REMARKS

This application is believed to be in condition for allowance at the time of the next Official Action.

Claim 5 is amended.

Claims 1-21 remain pending in the application.

Claims 7-21 are withdrawn from consideration as being directed to a non-elected invention.

Claim 5 was rejected under 35 USC 112, second paragraph, as being indefinite.

Specifically, the Official Action stated that claim 5 was confusing as to how the mononuclear derived cells in claim 5 are related to the mononuclear derived cells in the base claim 1. Applicants respectfully submit that claim 5 has been amended in a manner that is definite, and it is clear that claim 5 is directed to a method of obtaining monocyte derived cells (i.e. as administered in an effective amount in claim 1).

Therefore, applicants respectfully request that the indefiniteness rejection be withdrawn.

Claims 1, 2 and 4-6 were rejected under 35 USC 103(a) as being unpatentable over BARTHOLEYNS et al. Immunobiology, 1996, vol. 195, pages 550-562 (BARTHOLEYNS). Applicants respectfully disagree.

The present invention relates to a method for treating a patient suffering from a neoplasic or infectious disease, comprising administering an effective amount of monocyte derived

cells and an effective amount of chemotherapy drugs to said patient.

In a preferred embodiment, the two active ingredients are administered simultaneously and are in the form of an injectable solution.

The article of BARTHOLEYNS et al. reports the results of clinical trials using activated macrophages (i.e., MAK cells) in adoptive immunotherapy treatments. In the context of these observations, the immunotherapy appears as a new approach for treating cancer and requires standardized procedures (see page 555 and 557).

At page 557, BARTHOLEYNS suggests that "stimulation of the immune response against established tumors might only be successful when the tumor burden has been reduced to manageable proportions by prior surgery, chemo- or radiotherapy".

In other words, BARTHOLEYNS states that immune response is not sufficient against established tumors to cause major regression of tumor mass. Rather, the article suggests treating the tumors to reduce the tumor mass before even beginning treatment with activated macrophages.

This article does not disclose any therapy including the administration in a patient of an effective amount of monocyte derived cells (i.e., a cell distinct from activated macrophages) and an effective amount of chemotherapy drugs as

recited in claim 1. Thus, this article does not cite the method claimed in the patent application.

Moreover, there would be no motivation to modify BARTHOLEYNS to arrive at the recited method. When reading the article of BARTHOLEYNS, a person skilled in the art of treating cancer would immediately think about the apparent contradiction of administering a cellular preparation (e.g. monocyte derived cells) along with a treatment designed to limit or stop the cell life (e.g. chemotherapy). Indeed, one would expect chemotherapy to limit growth or kill the monocyte derived cells. Therefore, the general assertion made in the Official Action does not constitute a serious motivation for combining chemotherapy and cellular therapy as claimed in the present invention.

Moreover, in this article no results are shown about a possible action of the monocyte derived cells and chemotherapy drugs. In fact, the first results about this association were obtained *in vitro*. These results are presented in the example 1 (page 11) of the present application.

Briefly, two ovarian tumor cell lines were used to study combined effects of cisplatin (chemotherapy drug) and macrophage cells. These experiments demonstrated that the combined cytotoxic effects of macrophages and cisplatin are more important than the addition of both effects of cisplatin and macrophages when used separately. Thus an unexpected additive

effect exists between both treatments. This non-obvious result was never suggested before this study.

The Examiner's attention is respectfully directed to the appendix of this amendment. Included is the following evidence supporting the unexpected results exhibited by the claimed invention:

A declaration filed under Rule 132 regarding the results obtained during the clinical trials carried out on melanoma by M. Bartholeyns. This study demonstrates that even in patients with progressive stage IV advanced melanoma, the sequence of chemotherapy and monocytes derived dendritic therapy can achieve very significative clinical response.

Additional evidence of the unexpected results will be filed as a supplemental amendment:

a) A declaration filed under Rule 132 regarding the results for clinical study by Jean-Marie Dupuy. A phase II study demonstrates the safety and efficacy of combined treatment (association chemotherapy/macrophage cells) in ovarian cancer patients.

b) A note from Dr. C. Louvet (in French and with its English translation) that identifies the patents in the study on activated macrophages and chemotherapy.

The Examiner is asked to contact the undersigned should there by any questions regarding the declarations.

As further demonstrated in example 1 of the present application, the combination of macrophages and cisplatin allows to suppress the cells resistance to the chemotherapeutic drug. This is surprising, because of the possible cytotoxic effect of cisplatin on the macrophages themselves, which was not observed the conditions of the invention. Furthermore, the combination of chemotherapeutic drugs and activated macrophages allows to solve the acute problem of drug resistance in cancer treatment by chemotherapy.

The present patent application shows, that contrary to the prejudgement, it is possible to observe an efficient killing of tumor cells by associating cellular therapy and chemotherapy.

Therefore, in view of the above, applicants respectfully request that the obviousness rejection be withdrawn.

Claim 3 was rejected under 35 USC 103(a) as being unpatentable over BARTHOLEYNS further in view of GEHL et al. (GEHL). Applicants respectfully disagree.

GHEL studies the effect of the combination doxorubicin/paclitaxel (Taxol; Bristol-Myers Squibb Company) on metastatic breast cancer.

Taxol and doxorubicin are chemotherapy drugs well known in the art.

In the article of GEHL, the results show that the combination of doxorubicin and paclitaxel could play a role in treating symptomatic and aggressive disseminated breast cancer.

For the reasons discussed previously, a person skilled in the art would not have combined the teachings of BARTHOLEYNS and a chemotherapy drug, such as those of GEHL, for treating cancer.

None of these documents suggests a method for treating a patient suffering from a neoplasic or infectious disease comprising the administration of an effective amount of monocytes derived cells and of an effective amount of chemotherapy drugs to said patient.

Therefore, applicants respectfully request that the rejection be withdrawn.

In view of the foregoing Remarks, applicants believe that the present application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

- Declaration Under Rule 132 of Jacques Bartholeyns